

1. Èvorišèec D, Èeoviaè S, Boršo G, Rukavina AS. Endemic nephropathy in Croatia. *Clin Chem Lab Med* 1998;36:271-7.
Institute of Clinical Laboratory Diagnosis, Zagreb University School of Medicine Hospital Center, Zagreb, Croatia
Endemic nephropathy is a chronic renal disease with a high prevalence in a geographically limited area of Croatia. It has also been recorded in some parts of Bosnia, Serbia, Bulgaria and Romania. Despite numerous studies conducted to date, the etiology of this disease has not been clarified. Pathological studies of the kidney in the early stage of endemic nephropathy have shown renal tubules to be the primary sites of the pathologic process with an interstitial tissue reaction, whereas glomerular alterations are of a secondary character. Tubulointerstitial lesions can thus account for the symptoms of the disease, i.e., tubular proteinuria and reduced urine concentration capacity and urine acidification. Also, an increased incidence of malignant tumors of the urinary tract was found in the same geographic area.
2. *Gajoviaè S, Chowdhury K, Gruss P. Genes expressed after retinoic acid-mediated differentiation of embryoid bodies are likely to be expressed during embryo development. *Exp Cell Res* 1998;242:138-43.
*Zagreb University School of Medicine, Department of Histology & Embryology, Zagreb, Croatia
In order to test if retinoic acid-mediated differentiation of embryoid bodies can be used as an in vitro preselection method for ES cell lines generated by gene trap, we correlated gene expression after in vitro differentiation and in 11.5-day embryos. Fifty-two genes captured by gene trap and expressed in undifferentiated embryonic stem cells were analyzed. Most genes expressed after differentiation in vitro were also expressed during embryo development. In order to correlate the expression patterns in vitro and in vivo, the in vitro expression in the center and in the periphery of the embryoid body outgrowths was observed. This allowed us to distinguish, according to in vitro expression, not expressed genes from those expressed widely in 11.5-day embryos. This study demonstrates the potential of the differentiation procedure in combination with the gene trap to select in vitro for genes expressed during embryo development.
3. *Karavaniaè I, Smith FH. The Middle/Upper Paleolithic interface and the relationship of Neanderthals and early modern humans in the Hrvatsko Zagorje, Croatia. *J Hum Evol* 1998;34:223-48.
*Department of Archaeology, Faculty of Philosophy, University of Zagreb, Croatia
This paper presents the first detailed analysis of the artifacts from the Mousterian level G3 at Vindija Cave and a revision of the artifact analysis for the early Upper Paleolithic levels at Velika Peæina, both in Croatia. Combined with an assessment of the artifacts from the crucial G1 level at Vindija, results of these analyses are used to argue that the combination of Middle and Upper Paleolithic elements in the upper G complex at Vindija is not necessarily the result of geological mixing but may well represent a natural cultural assemblage. Some Upper Paleolithic elements are possibly derived from the local Mousterian, while others result from extraneous cultural influences into this region. Interestingly, currently available radiocarbon dates indicate that Neanderthals (Vindija level G1) and early modern humans (Velika Peæina) were penecontemporaneous in this region at ca. 33 ka, or perhaps somewhat earlier if the radiocarbon dates are taken as minimum age estimates.
4. Ljubiæ S, Metelko Z, Car N, Rogliæ G, Dražiæ Z. Reduction of diffusion capacity for carbon monoxide in diabetic patients. *Chest* 1998;114:1033-5.
Vuk Vrhovac Institute, University Clinic for Diabetes, Endocrinology & Metabolic Diseases, Zagreb, Croatia
This study demonstrates the relationship between pulmonary and other chronic complications in diabetes. Twenty-seven patients with diabetes, aged 21 to 62 years, who had had the disease from 3 to 32 years, were included in this study. The protein excretion rate (PER) and the diffusion capacity of the lung for carbon monoxide (DLCO) were included as parameters of the severity of complications. The variables of age, duration of diabetes, and complication

parameters were included in a multiple regression model with forward, stepwise selection to assess their value in predicting DLCO/VA. The variables were found to be significant predictors of DLCO/VA ($R^2=0.46$, adjusted $R^2=0.32$, $p<0.022$). However, proteinuria was the only significant independent predictor of DLCO/VA. This finding indicates that both renal and pulmonary complications of diabetes share a similar microangiopathic background.

5. Mašić N, Gagro A, Rabatić S, Sabioncello A, Dašić G, Jakšić B, Vitale B. Decision-tree approach to the immunophenotype-based prognosis of the B-cell chronic lymphocytic leukemia. *Am J Hematol* 1998;59:143-8.
Division of Molecular Medicine, Rudjer Bošković Institute, Zagreb, Croatia
In this work, decision-tree approach to cell phenotype-based prognosis of CLL was adopted. The panel of 33 parameters was simultaneously presented to the C4.5 decision tree which extracted the most informative of them and subsequently performed classification of CLL patients against the modified Rai staging system. It has been shown that substantial correlation between the percentage of expression of the CD23 molecule on CD19+ B-cells, the level of sCD23, the percentage of CD45RA+, and the absolute number of CD4CD45RA+RO+ T-cells and the clinical stages, exists. The prediction vector, composed of their concatenated values, correctly associated 83% of the cases in the low-risk group (Rai stage 0), 100% of the cases in the intermediate-risk group (Rai stage I and II), and 89% of the cases in the high-risk group (Rai stage III and IV) of CLL patients. It may be inferred that two processes play important roles in the progression rate of CLL: 1. deregulated function of the CD23 gene in B-cells accompanied by the appearance of its cleaved product sCD23 in the sera; and 2. functionally impaired and imbalanced CD4 T-cell subpopulations found in the peripheral blood of CLL patients.
6. McCallum JB, *Boban N, Hogan Q, Schmeling WT, Kampine JP, Bošnjak ZJ. The mechanism of alpha2-adrenergic inhibition of sympathetic ganglionic transmission. *Anesth Analg* 1998;87:503-10.
*Department of Epidemiology, Split University School of Medicine, Split, Croatia
In this study, we examined the effects of dexmedetomidine (DMT), an alpha2-agonist, on neural conduction and neurotransmitter release in sympathetic ganglia. The stellate ganglia from 48 mongrel dogs were isolated, desheathed, and superfused with Krebs' solution. DMT dose-dependently inhibited synaptic transmission with a 50% effective dose of 71.6 (26.0-174.3) mM. Neurotransmitter release was reduced 25% by 70 mM DMT during low-frequency (0.4 Hz) stimulation, but this effect was abolished at higher frequency (5 Hz) stimulation. DMT inhibited the excitatory postsynaptic response to exogenous muscarinic stimulation but not nicotinic stimulation. These results indicate that alpha2-receptor activation depresses ganglionic transmission through postsynaptic inhibition of muscarinic stimulation, although reduction of neurotransmitter release through a presynaptic auto-feedback mechanism is also involved. Our study indicates that the central sympatholytic effects of alpha2-adrenoceptor stimulation are augmented by peripheral inhibition of ganglionic transmission.
7. Mijić A, Ferenić Z, Belicza M, Fučić A, Šević SR, Šarčević B, et al. Apoptosis in human gastric polyps and adenocarcinomas: a stereological analysis. *Hepatogastroenterology* 1998;45:684-90.
Department of Surgery, University Hospital Sestre Milosrdnice, Zagreb, Croatia
The occurrence of apoptotic cells was analyzed in human normal gastric mucosa, polyps and adenocarcinomas. The counting of apoptotic cells was performed using the 40x objective with a calibrated eyepiece Weibel's multi-purpose M42 stereological test system. Each group was evaluated stereologically, determining numeric density of apoptotic cells. There was progressive and statistically significant increase of apoptotic numeric densities from normal gastric epithelium to adenomatous polyp and, finally, to cancer. Carcinomas with metastasis contained higher number of apoptotic cells than without metastasis. Gastric cancer could be separated in three statistically different groups: a) intestinal type gastric cancer with metastasis (the highest number of apoptotic cells); b) intestinal type gastric cancer without metastasis and diffuse gastric cancer with metastasis (medium number); and c) diffuse type gastric cancer without metastasis, mixed gastric cancer with and without metastasis (the lowest number of apoptotic cells). Our results suggest that numeric densities of apoptotic cells are associated with tumor progression in human gastric carcinogenesis and can be used as prognostic mark.
8. *Poljić B, Hengel H, Krmpotić A, Trgovčich J, Pavić I, Luccaroni P, et al. Hierarchical and redundant lymphocyte subset control precludes cytomegalovirus replication during latent infection. *J Exp Med* 1998;188:1047-54.

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We took advantage of latently infected B cell-deficient mice and a sensitive method for virus detection to study CMV reactivation after ablation of lymphocyte subsets. Within 5 d after depletion of lymphocytes, productive infection occurred in 50% of mice, and 14 d later 100% of mice exhibited recurrent infection. A hierarchy of immune control functions of CD8+, NK and CD4+ cells was established. Reactivation was rare if only one of the lymphocyte subsets was depleted, but was evident after removal of a further subset, indicating a functional redundancy of control mechanisms. The salivary glands were identified as the site of most rapid virus shedding, followed by the detection of recurrent virus in the lungs, and eventually in the spleen. Our findings document a previously unknown propensity of latent CMV genomes to enter productive infection immediately and with a high frequency after immune cell depletion. The data indicate that only the sustained cellular immune control prevents CMV replication and restricts the viral genome to a systemic state of latency.

9. Požgain I, Mandić N, Barkić J. Homicides in war and peace in Croatia. *J Forensic Sci* 1998;43:1124-6.

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This work shows the interdisciplinary investigation of homicides in the Osijek area during the war and prewar periods. Similarities between the prewar and wartime perpetrators are related to social-demographic characteristics. Significant differences are found in the homicidal method of selection among victims and participation of victims involved. The major contributing factors in homicide genesis were acute alcohol intoxication and personality disorder among perpetrators. Besides these factors, the war stressors and access to firearms were significant factors during the war homicides. Prevention efforts should be directed toward consequential measures and further investigation suggests that the emphasis must be put on victimological aspects of the homicide problem.

10. Paralkar VM, Vail AL, Grasser WA, Brown TA, Xu H, *Vukičević S, et al. Cloning and characterization of a novel member of the transforming growth factor-beta/bone morphogenetic protein family. *J Biol Chem* 1998;273:13760-7.

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We cloned a novel member of the bone morphogenetic protein (BMP) family that is expressed at high levels in the placenta and the prostate and that we have designated as prostate-derived factor (PDF). Based on cDNA sequence analysis, the predicted PDF protein contains two cysteines in addition to the seven conserved cysteines that are the hallmark of the members of the TGF-beta superfamily. In addition, Northern blot hybridization to poly(A)+ RNA showed low levels of expression in the kidney and pancreas. High expression of the protein was found in the terminal villi of the placenta. In day 18 rat embryos, protein expression was also seen in the skin and in the cartilaginous tissue of developing skeleton. Orchidectomy and dihydrotestosterone treatment of rats revealed that PDF expression is regulated by androgens in the prostate. Subcutaneous implantation of recombinant PDF induced cartilage formation and the early stages of endochondral bone formation. These data indicate that PDF has a functional relationship to the BMPs.

11. *Rukavina D, Laškarin G, Rubeša G, Štrbo N, Bedenicki I, Manestar D, et al. Age-related decline of perforin expression in human cytotoxic T lymphocytes and natural killer cells. *Blood* 1998;92:2410-20.

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Flow cytometric technique for detecting cytoplasmic perforin (P) has been used to quantify age-related changes in perforin expression in human peripheral blood lymphocytes (PBL). Proportions of P+ lymphocytes increased after birth, but declined rapidly after the age of 70 years. This was true for both T cells and CD16+ and CD56+ natural killer (NK) cells. Children showed in addition to high levels of perforin positive CD8+ cells a much higher proportion of CD4+ P+ cells than the other age groups. In elderly individuals there was also a highly significant reduction in mean levels of perforin per cell as compared with all other groups. Adult women had consistently higher mean levels of perforin per cell than adult men for all P+ cell phenotypes. Functional tests clearly showed the deficiency in early spontaneous cytotoxic potential of PBL from elderly persons due to relative P deficiency, which can be corrected by stimulation of cytolytic cells with target cells and interleukin-2 (IL-2). The deficiency in cytolytic activity on the contact with target cells may have implications for antiviral and antitumor immunity in elderly persons.

12. Bagariæ I. La santé publique et al guerre en Bosnie- Herzégovine. Bulletin de santé publique 1998;19:1-5.
Mostar University School of Medicine, Mostar, Bosnia and Herzegovina
À la fin des années 80 et au début des années 90, les Républiques de Croatie, de Bosnie-Herzégovine et de Macédonie se sont auto-proclamées autonomes à la suite d'élections et de référendums. Elles devenaient indépendantes de la Yougoslavie. En dépit de la reconnaissance internationale de l'indépendance de ces républiques par la plupart des pays d'Europe et d'ailleurs, la Serbie et l'armée nationale yougoslave ont mené une longue guerre en vue de maintenir le vieux régime communiste et ralentir la tendance aux changements vers la démocratie. Face aux attaques de l'artillerie lourde et des tanks, des centaines de milliers de personnes ont fui leurs villes afin de sauver leur vie et celle de leur famille. Des flots de réfugiés se sont déversés en République de Croatie où environ cinq cent mille (500 000) personnes de Bosnie-Herzégovine ont trouvé refuge. Pendant que des réfugiés de Bosnie-Herzégovine déguerpissaient vers l'Europe, et vers d'autres pays de monde. Beaucoup de réfugiés se sont également dirigés vers une partie du territoire de la Bosnie-Herzégovine non occupée. En état de choc, blessés et démunis, les réfugiés avaient été chassés de leurs fermes de l'Est et du Nord-Est de la Bosnie. Un peu moins de la moitié de la population d'avant guerre de la Bosnie-Herzégovine a été déracinée. Des gens d'Europe et du monde entier qui avaient visité Medugorije (lieu de pèlerinage où la Vierge est apparue) avant et durant la guerre ont apporté de l'aide en supportant les églises ou les organisations caritatives. De même des organisations humanitaires internationales, particulièrement Médecins sans frontières, les Nations-Unies, le Haut Commissariat pour les Réfugiés (HCR) et l'UNICEF ainsi que la Croatie se sont également manifestés par leur support. De nombreux médicaments ont été donnés. Toutefois, lorsque ces médicaments parvenaient à destination, une grande partie de ceux-ci étaient devenus inutilisables parce qu'ils étaient périmés. Il était aussi courant d'avoir des produits chimiques non-médicaux et des fournitures médicales impropres. Leur accumulation a créé des problèmes d'entreposage et d'évacuation des déchets. Nous avons un taux de chômage extrêmement élevé (80%). Des investissements sont nécessaires tout comme de l'aide en éducation pour les jeunes générations, leur apprendre à soigner, comment se procurer de la nourriture, des vêtements et un abri, comment développer des infrastructures de base de santé publique et de survie. En un mot, comment remettre un pays et son peuple sur pied.
13. *Skalko N, Peschka R, Altenschmidt U, Lung A, Schubert R. pH-sensitive liposomes for receptor-mediated delivery to chicken hepatoma (LMH) cells. FEBS Lett 1998;434:351-6.
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pH-sensitive liposomes composed of dioleoylphosphatidylethanolamine and cholesterol hemisuccinate (3:2 mol/mol) bearing the N-acetylglucosamine derivative of bovine serum albumin (N-Ac-BSA) were applied for receptor-mediated delivery in chicken hepatoma (LMH) cells expressing the N-Ac-BSA-binding asialoglycoprotein receptor. Fluorescently labeled dextran was entrapped in liposomes by a modified freeze-thawing method (encapsulation efficiency of 23%). A novel method of coupling proteins onto the surface of preformed liposomes yielded a coupling efficiency of 60-70%. The association of pH-sensitive and lecithin liposomes with LMH cells was monitored by fluorescence-activated cell sorting and confocal microscopy. Prerequisites for receptor-mediated delivery to LMH cells were both the pH sensitivity of liposomes and the presence of N-Ac-BSA on the liposomal surface.
14. Stanec S, Stanec Z. Ulnar nerve reconstruction with an expanded polytetrafluoroethylene conduit. Br J Plast Surg 1998;51:637-9.
Department of Plastic Surgery, University Hospital Dubrava and Zagreb University School of Medicine, Zagreb, Croatia
The ulnar nerve of a 22-year-old woman was reconstructed by expanded polytetrafluoroethylene (ePTFE) conduit, 141 days after nerve transection at the distal forearm level. A 2.9 cm nerve gap was bridged by a corrugated, 3.9 cm long, 6 mm diameter ePTFE tube. At final evaluation 3 years later, the patient achieved excellent motor and sensory recovery. Exploration of the tube, at that time, showed macroscopically normal nerve inside the conduit.
15. Stanimiroviæ A, *Skerlev M, Stipiæ T, Beck T, Basta-Juzbašić A, Ivankoviæ D. Has psoriasis its own characteristic trichogram? J Dermatol Sci 1998;17:156-9.
Department of Dermatology & Venerology, Zagreb University School of Medicine, Zagreb, Croatia
The aim of this study was to determine if there were characteristic trichogram changes in scalp psoriasis in patients without clinically evident effluvium or alopecia. A total of 45 patients

(17 men and 28 women, aged from 15 to 73 years) with clinically and histologically confirmed psoriasis vulgaris with scalp involvement were included. The control group consisted of 60 volunteers with no scalp involvement. Our results from the psoriatic group showed highly increased proportions of dysplastic hair roots. Median proportion was 50% with 95% confidence interval (CI) for median 30-60%, whereas telogen hair ratio was slightly increased – median proportion was 16% with 95% CI for median 15-20%. Within the psoriasis patients' group no statistically significant correlations were found between the proportion of dysplastic hairs and the patients' age, sex, and the intensity and duration of disease. The increased proportion of dysplastic hairs in scalp psoriasis without effluvium or alopecia might be its characteristic trichogram sign.

16. *Užareviæ B, Petroveèki M, Marušiæ M, Jakiæ-Razumoviæ J, Hutinec Z, Sabioncello A, et al. Prognostic significance of cell cycle parameters in infiltrative ductal breast carcinoma. J Clin Lab Anal 1998;12:131-6.

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Flow-cytometric DNA analysis was performed retrospectively from paraffin-embedded blocks in 158 consecutive ductal infiltrative breast carcinoma patients grades I-III. Normal breast tissue was used as control. Tumor proliferative activity, cell ploidy, and DNA index (DI) were related to age of patients, histological grade of tumor, tumor size, axillary lymph node status, estrogen and progesterone receptor status, menopausal status, TNM clinical classification, and survival. There was a significant association between DNA aneuploidy and a high cellular proliferative activity, increased DI, poor differentiation of tumor, primary tumor size, number of positive lymph nodes, and postmenopausal state. Increased proportion of cells in S-phase was associated with positive lymph node status and higher number of positive lymph nodes. The cell cycle parameters had no prognostic value either for overall survival or disease-free survival of the patients.